REMARKS/ARGUMENTS

Claims 1-16 are currently pending. Claims 1, 2, 6, 9, 10, 13 and 16 have been amended. Claim 5 has been canceled. Claims 17-20 were previously withdrawn. Applicants respectfully request entry of this amendment based on the following remarks.

Rejection under 35 USC 102(b)

The Examiner rejected claims 1-3, 9 and 10 as anticipated by reference US 2002/0049152 (Nock et al.).

The Examiner rejected the claims on the basis that the reference teaches a method of immobilizing a polypeptide to a surface using mutant inteins by expressing a chimeric gene encoding a fusion protein that comprises a polypeptide and an intein and then attaching anchor molecules to the polypeptides and anchoring the polypeptides to a surface.

Claims 1 and 9 have been amended to incorporate features of former claims 5 and 13, namely that the ligand is cysteine-biotin and the attaching of the cysteine-biotin occurs by reacting the fusion protein containing the mutated intein with the cysteine-biotin. Claims 1 and 9 have also been amended to specify that the cysteine-biotin is attached to the C-terminus of the remaining portion of the fusion protein via a peptide bond so that the biotin moiety is attached to the backbone of the fusion protein. Former claim 5 has been canceled and former claim 13 has been amended to delete the feature incorporated into claim 9. Support for these amendments can be found at least in claims 2, 5, 10 and 13, at paragraphs [0029], [0035], [0040], [0042], [0053] and [0054], and in Figure 1 of the application as originally filed.

Claims 1 and 9 as amended now specify the feature of claims 5 and 13, namely that the ligand is cysteine-biotin. The Examiner did not object to claims 5 and 13 as anticipated by Nock et al., and specifically stated at the bottom of page 4 of the Office

Action that Nock et al. fails to teach that the ligand is cysteine-biotin. The remaining cited claims, claim 2, 3 and 10, depend directly or indirectly from claim 1 or claim 9. Applicants therefore respectfully submit that the claims as amended are not anticipated by Nock et al.

Rejection under 35 USC 103

The Examiner rejected claims 4-8 and 11-16 as obvious having regard to the Nock et al. reference in view of one or more of Duan, Xu et al., Bradley et al. and Inoue et al.

Particularly, the Examiner stated that with respect to claims 5 and 13, Xu et al. teaches a biotinylated peptide possessing an N-terminal cysteine.

Applicantly respectfully disagrees that the cited combinations of references render the currently claims obvious, for at least the following reasons.

The claims as currently amended require that the ligand is cysteine-biotin and that the cysteine-biotin is attached to the newly generated C-terminus of the fusion protein so that the biotin is attached to the backbone of the protein. As stated in paragraph [0042] of the application and as can be readily seen from Figure 1 of the application, cysteine-biotin has the biotinyl moiety attached to the C-terminus of a single cysteine residue via a peptide bond. The resulting cleavage of the fusion protein and attachment of cysteine-biotin to the newly generated C-terminus of the fusion protein results in a protein having one additional cysteine residue followed by a biotinyl moiety attached via peptide linkages to the backbone of the protein.

As stated in paragraph [0035] of the application as originally filed, it is advantageous to immobilize proteins in an array in such a manner that the proteins retain their native activity within the array. The presently claimed methods result in attachment of small ligands having only a single amino acid residue and a biotinyl moiety attached to the C-terminus of a protein, thus reducing the potential for disruption of the protein activity when the protein is immobilized in an array. As well,

the small size of the cysteine-biotin ligand and the attachment of the ligand so that the biotin is linked to a protein backbone via a peptide linkage provides a specific, ordered orientation of the protein within the array.

The above-described features of the presently claimed methods are not provided by any combination of the cited references, including in particular Nock et al. combined with Xu et al.

Specifically, Xu et al. describes a septapeptide having an N-terminal cysteine in which the side-chain of lysine is modified with a biotin residue (see column 7, lines 11-15 of Xu et al.). Thus, the ligand described by Xu et al. is a biotinylated peptide that is not a cysteine-biotin, and that is significantly longer than a single cysteine residue attached to a biotinyl moiety. Furthermore, the end result of modification with the biotinlyated peptide of Xu et al. is that a biotin residue is attached to a protein of interest via a side-chain of the protein, influencing the orientation of the protein when immobilized in a protein array.

Given that the claims of the instant application as amended specify cysteine-biotin, not a biotinylated peptide, and given that the cysteine-biotin is structured so that the biotin is attached to the C-terminus of the cysteine via a peptide bond (as can be seen in Figure 1 and in paragraph [0042] of the instant application), ultimately resulting in attachment of the biotinyl moiety to protein of interest via a peptide bond, Xu et al. does not describe or suggest the features of the present claims.

Applicant further submits that the remaining references, Duan, Bradley et al. and Inoue et al. do not overcome the above-described deficiency of Xu et al., even in combination with Nock et al. Thus, none of the references cited under 35 USC 103 can combine with Nock et al. and Xu et al. to render as obvious the present claims as currently amended. Applicants respectfully request withdrawal of this rejection.

It is believed that no new matter has been added by these amendments.

In view of the foregoing, it is believed that the application is in condition for allowance. Applicants respectfully request entry of this amendment and allowance of the application.

Respectfully submitted,

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